

DOCKET NO.: L0559.70001US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Newman et al.  
Serial No.: 09/507,146  
Confirmation No.: 8881  
Filed: February 18, 2000  
U.S. Patent No.: 6,869,606 B1  
Date of Patent: March 22, 2005  
For: BIOTINYLATED-CHEMOKINE ANTIBODY COMPLEXES  
Examiner: Canella, Karen A.  
Art Unit: 1642

**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to Attention: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 11, 2005.

  
Nicole Millette Hawes

**Attention: Certificate of Correction Branch**  
Commissioner For Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**REQUEST FOR CERTIFICATE OF CORRECTION**  
**UNDER 37 C.F.R. § 1.322 and § 1.323**

Sir:

Applicants respectfully request the correction of errors in the claims found in the printing of U.S. Patent 6,869,606 B1.

**Remarks**

Applicants enclose herewith a copy of the error-containing pages from patent US 6,869,606 B1, with the errors marked in red. Some of the errors are errors on the part of the PTO. The error in Claim 65 is an error on the part of the Applicants. This error occurred in good faith and without deceptive intention and correction of this mistake would neither constitute new matter nor require reexamination. The fee of \$100.00 under 37 C.F.R. §1.20(a) is enclosed.

Applicants respectfully request a Certificate of Correction for the errors outlined herein.

Respectfully submitted,

04/14/2005 AWONDAF1 00000029 6869606

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Docket No.: L0559.70001US00  
Date: April 11, 2005  
xNDDx



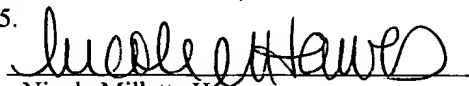
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Alexandria, VA 22313-1450

Sir:

Transmitted herewith are the following documents:

- Request for Certificate of Correction
- Certificate of Correction
- Copy of pages of USPN 6,869,606 with corrections marked in red.
- Return Receipt Postcard

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 646-8000, Boston, Massachusetts.

A check in the amount of \$100 is enclosed. If any additional fees are required, the Commissioner is hereby authorized to charge Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

Respectfully submitted,



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UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : US 6,869,606 B1

DATED : March 22, 2005

INVENTOR(S): Newman et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In claim 15, column 36, lines 16 and 17 delete "lympholactin" and insert therefor -- lympholactin --.

In claim 30, column 36, line 55 delete "1-309," and insert therefor -- I-309, --.

In claim 65, column 38, line 26 delete "chemokine is chemokine" and insert therefor -- chemokine is a chemokine --.

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PATENT NO. US 6,869,606 B1



TABLE 5-continued

Double-Agent Cross-linker	Reactive Towards								
	—NH <sub>2</sub> —SH		Carbohydrates	Non-selective (Photo- reactive)	—COOH	Cleavable By			
	Acronym	Aminos	Sulphydryls			Carboxyls	Thiols	Base	Periodate Hydroxylamine
Sulfo-SMBP		X	X						
Sulfo-LC-SMPT		X	X						

What is claimed is:

1. A composition comprising:

(a) a biotin conjugate comprising:

(i) a biotin covalently coupled to

(ii) a pharmacologically active chemokine; and

(b) an anti-biotin antibody selectively bound to said biotin to form a complex.

2. The composition of claim 1, wherein the pharmacologically active chemokine has an agonist activity.

3. The composition of claim 1, wherein the pharmacologically active chemokine has an antagonist activity.

4. The composition of claim 1, wherein the complex has a half-life ranging from about 15 minutes to about 1 hour in the presence of supra physiological levels of biotin and the anti-biotin antibody has an affinity constant ranging from about 1.0 to about 100.0 nanomolar.

5. The composition of claim 1, wherein the anti-biotin antibody comprises a therapeutic agent that is a cytotoxic agent.

6. The composition of claim 1, wherein the anti-biotin antibody comprises a diagnostic agent attached thereto.

7. The composition of claim 1, wherein the anti-biotin antibody has a dual specificity.

8. The composition of claim 7, wherein the anti-biotin antibody selectively binds to a tumor cell associated antigen.

9. The composition of claim 7 wherein the anti-biotin antibody selectively binds to a viral associated antigen.

10. A composition comprising:

(a) a biotin conjugate comprising

(i) a biotin covalently coupled to

(ii) a chemokine having a pharmacological activity; and

(b) a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier is suitable for parenteral administration.

11. The composition of claim 1, wherein the composition is lyophilized.

12. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

13. The composition of claim 12, wherein the pharmaceutically acceptable carrier is acceptable for a mode of delivery selected from the group consisting of: intradermal delivery, intramuscular delivery, intraperitoneal delivery, intravenous delivery, subcutaneous delivery, and controlled release delivery.

14. The composition of claim 1, wherein the biotin is selected from the group consisting of L-biotin, D-biotin and derivative thereof.

15. The composition of claim 1, wherein the chemokine is selected from the group consisting of the chemokines RANTES, MIP-1alpha, MIP-1 beta, MCP-1, MCP-2, MCP-3, MCP-4, eotaxin, eotaxin-2, TARC, MDC, MIP-3alpha, MIP-3beta, I-309, HCC-1, HCC-2, MIP-3, MIP-4, SLC, TECK, LEC, CKb-15, PTEC, IL-8, GROalpha, GRObeta,

15 GROgamma, PF4, NAP-2, ENA-78, GCP2, IP-10, MIG, ITAC, MIP-2, CKa2, ADEC, SDF, fractalkine and lympholactin.

16. The composition of claim 1, wherein the chemokine has a carboxyl terminus and the biotin is covalently attached to the carboxyl terminus of the chemokine.

17. The composition of claim 1, wherein the biotin is covalently coupled to the pharmacologically active chemokine via a linker molecule.

18. The composition of claim 1, wherein the complex has a half-life ranging from about 15 minutes to about 1 hour in the presence of supra physiological levels of biotin.

19. The composition of claim 1, wherein the anti-biotin antibody has an affinity constant ranging from about 1.0 to about 100.0 nanomolar.

20. The composition of claim 1, wherein the anti-biotin antibody is selected from the group consisting of an intact antibody, and an antibody fragment.

21. The composition of claim 1, wherein the anti-biotin antibody is a human antibody or fragment thereof.

22. The composition of claim 1, wherein the anti-biotin antibody has a subclass selected from the group consisting of a IgG1 subclass, and an IgG3 subclass.

23. The composition of claim 1, wherein the anti-biotin antibody comprises a therapeutic agent attached thereto.

24. The composition of claim 1, wherein the complex has a half-life of from one day to one month in vivo.

25. The composition of claim 1, wherein the complex has a half-life of from one week to two weeks in vivo.

26. The composition of claim 10, wherein the chemokine having a pharmacological activity has an agonist activity.

27. The composition of claim 10, wherein the chemokine having a pharmacological activity has an antagonist activity.

28. The composition of claim 10, wherein the composition is lyophilized.

29. The composition of claim 10, wherein the biotin is selected from the group consisting of L-biotin, D-biotin and derivative thereof.

30. The composition of claim 10, wherein the chemokine is selected from the group consisting of the chemokines RANTES, MIP-1 alpha, MIP-1 beta, MCP-1, MCP-2, MCP-3, MCP-4, eotaxin, eotaxin-2, TARC, MDC, MIP-3alpha, MIP-3beta, I-309, HCC-1, HCC-2, MIP-3, MIP-4, SLC, TECK, LEC, CKb-15, PTEC, IL-8, GROalpha, GRObeta, GROgamma, PF4, NAP-2, ENA-78, GCP2, IP-10, MIG, ITAC, MIP-2, CKa2, ADEC, SDF, fractalkine and lympholactin.

31. The composition of claim 10, wherein the chemokine has a carboxyl terminus and the biotin is covalently attached to the carboxyl terminus of the chemokine.

32. The composition of claim 10, wherein the biotin is covalently coupled to the chemokine having a pharmacological activity via a linker molecule.

33. The composition of claim 1, wherein the chemokine is ITAC.

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34. The composition of claim 1, wherein the chemokine is eotaxin.
35. The composition of claim 1, wherein the chemokine is MDC.
36. The composition of claim 1, wherein the chemokine is MIP-3alpha.
37. The composition of claim 1, wherein the chemokine is MIP-2.
38. The composition of claim 1, wherein the chemokine is MIP-1beta.
39. The composition of claim 1, wherein the chemokine is MCP-1.
40. The composition of claim 1, wherein the chemokine is MIP-1alpha.
41. The composition of claim 1, wherein the chemokine is RANTES.
42. The composition of claim 1, wherein the chemokine is I-309.
43. The composition of claim 10, wherein the chemokine is ITAC.
44. The composition of claim 10, wherein the chemokine is eotaxin.
45. The composition of claim 10, wherein the chemokine is MDC.
46. The composition of claim 10, wherein the chemokine is MIP-3alpha.
47. The composition of claim 10, wherein the chemokine is MIP-2.
48. The composition of claim 10, wherein the chemokine is MIP-1beta.
49. The composition of claim 10, wherein the chemokine is MCP-1.
50. The composition of claim 10, wherein the chemokine is MIP-1alpha.
51. The composition of claim 10, wherein the chemokine is RANTES.
52. The composition of claim 10, wherein the chemokine is I-309.

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53. The composition of claim 1, wherein the chemokine is a full-length chemokine.
54. The composition of claim 1, wherein the chemokine is a truncated chemokine.
55. The composition of claim 1, wherein the chemokine is an elongated chemokine.
56. The composition of claim 54, wherein the truncated chemokine is truncated at an amino terminus.
57. The composition of claim 54, wherein the truncated chemokine is truncated at a carboxy terminus.
58. The composition of claim 55, wherein the elongated chemokine is elongated at an amino terminus.
59. The composition of claim 10, wherein the chemokine is a full-length chemokine.
60. The composition of claim 10, wherein the chemokine is a truncated chemokine.
61. The composition of claim 10, wherein the chemokine is an elongated chemokine.
62. The composition of claim 60, wherein the truncated chemokine is truncated at an amino terminus.
63. The composition of claim 60, wherein the truncated chemokine is truncated at a carboxy terminus.
64. The composition of claim 61, wherein the elongated chemokine is elongated at an amino terminus.
65. The composition of claim 2 wherein the pharmacologically active chemokine is a chemokine truncated at the carboxy terminus.
66. The composition of claim 3, wherein the pharmacologically active chemokine is a chemokine truncated or elongated at the amino terminus.
67. The composition of claim 26, wherein the chemokine having a pharmacological activity is a chemokine truncated at the carboxy terminus.
68. The composition of claim 27, wherein the chemokine having a pharmacological activity is a chemokine truncated or elongated at the amino terminus.

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